Does Particulate Matter Cause or Exacerbate Asthma?

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research and development

Background

The EPA is uniquely positioned to lead and coordinate the national effort to determine the impact of air pollutants on asthma. In 2001, 20 million Americans (6.3 million children) had asthma. Asthma is the most common chronic childhood disease which costs $18 billion annually and disproportionately affects minorities and low-income populations.

Science Questions

- Does PM Exacerbate or Induce Asthma?
- Can Human Panel and Controlled Exposure Studies provide biological plausibility to explain the epidemiological findings?
- What are the mechanisms by which PM may exacerbate asthma?

Research Goals

- To characterize risks posed by ambient and indoor PM
- Identify risk factors which increases susceptibility to the effects of PM in asthma
- Identify biomarkers of response and susceptibility of asthmatics to PM
- Delineate mechanisms of action of PM in asthma
- Develop and test intervention strategies

Methods/Approach

Methods: A multifaceted, multidisciplinary approach is employed to assess the role of PM in asthma:

1. Epidemiological Studies: Used to characterize risks posed by ambient and indoor PM and identify the risk factors contributing to these effects in population studies of asthmatics
2. Panel Studies: Used to examine effects of ambient PM and air pollutants in well characterized asthmatic populations, often stratified on the basis of a biomarker or genotype identified in challenge studies
3. Human Challenge Studies: Used to identify biomarkers of susceptibility and response, identify potential mechanisms, and test potential personal intervention strategies (therapies)
4. Animal Studies: Used to examine mechanisms not feasible in human studies. Use of genetically modified mice, particle sources, or pharmacological tools not feasible in humans are a significant strength of this approach

General findings of the program to date:

1. PM induces inflammation in asthmatics
2. PM is linked with decreased lung growth
3. Endotoxin enhances airway inflammation, but is remediable with inhaled corticosteroid
4. Animal studies show that particles modify IgE sensitization

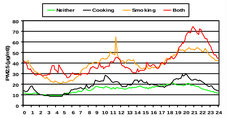
Epidemiological & Panel Studies

Inner-City Asthma Study

Within the NIH sponsored Inner-City Asthma Study (ICAS), EPA is collaborating in a study of indoor and outdoor particulate matter (PM) exposures and their association with the triggering of asthma attacks and other respiratory effects.

Results

Preliminary results in inner-city children with moderate to severe asthma suggest that day-to-day changes in indoor levels of fine particulate matter are associated with increased:
-Respiratory symptoms
-Medication use
-Clinic visits
-Hospitalizations



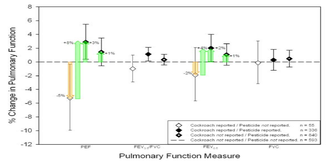
This chart shows the daily variation in indoor fine particle levels by category of home.

Indoor fine particle levels averaged:
- 15 μg/m³ in non-smoking homes
- 3.5 μg/m³ with smoky cooking events
- Tobacco smoking in the home nearly doubled the average levels to 39 μg/m3.

El Paso Children's Health Study

A study designed to examine border NO_2 levels and impact on asthma. No NO_2 effect, but cockroach exposure linked to decreased lung function in children

Expiratory Flow decreased with Cockroach Exposure, but increased with Pesticide Use in Home



Seattle Children's Study

Summary data of the effect of PM exposure on exhaled nitric oxide in a panel of asthmatic children not using inhaled corticosteroids vs. those who did in the Seattle region. Note the lack of impact on children using corticosteroids.

Table 2. Association between eNO (ppb) and $PM_{2.5}$ (μg/m³), winter and spring sessions, controlling for ambient NO and removing high outdoor NO days (> 100 ppb; $n = 19$).

	Change in eNO (95% CI) per 10 μg/m³ increase in $PM_{2.5}$	
Monitor	ICS nonuser ($n = 10$)	ICS user ($n = 9$)
Personal	4.48 (1.02–7.93)	−0.09 (−2.39 to 2.21)
Outdoor	4.28 (1.38–7.17)	0.74 (−2.28 to 3.76)
Indoor	4.21 (1.02–7.41)	−1.11 (−5.08 to 2.87)
Central site	3.62 (1.22–6.43)	1.28 (−1.23 to 3.79)

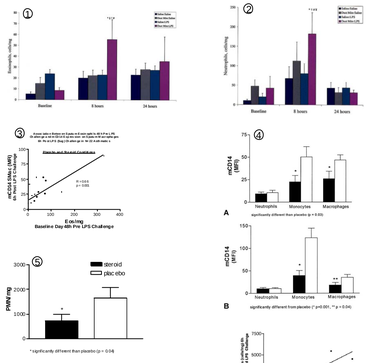
Controlled Human Exposure Studies

Endotoxin, a component of indoor and ambient air particles and bioaerosols, is associated with increased severity and induces airway inflammation in allergic asthmatics

Figures 1 & 2 demonstrate the synergistic action of sequential airway challenge with individually subthreshold of allergen and endotoxin on eosinophil and neutrophil influx.

Figure 3 shows the relationship between eosinophils and airway monocyte CD14.

Figures 4 & 5 show the effect of inhaled steroids on CD14 expression and PMN influx after endotoxin challenge.



The figures to the right indicate that CD11b expression on circulating monocytes correlates with endotoxin induced PMN influx

The figures below demonstrate that asthmatics have increased deposition of ultrafine particles relative to normal volunteers

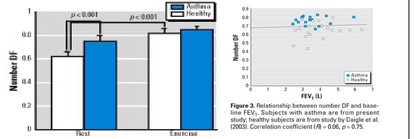
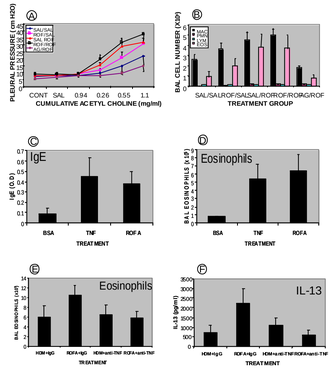


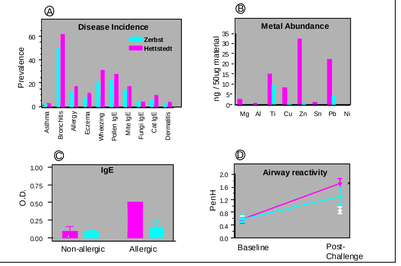
Figure 3. Relationship between number DF and baseline FEV_1. Subjects with asthma are from present study; healthy subjects are from study by Daigle et al. (2003). Correlation coefficient (r^2) = 0.66, $p < 0.75$.

Animal Studies

Rats exposed to residual oil fly ash have increased airway reactivity (A) and pulmonary eosinophils (B) during allergic sensitization to house dust mite allergic. This allergic adjuvancy can be reproduced with the pro-inflammatory cytokine TNF-α (C & D), and ameliorated by neutralizing this signaling molecule (E & F).



The rate of allergic disease is higher in the industrial town of Hettsted that Zerbst (Fig A) and this is associated with increased level of metals in $PM_{2.5}$ samples (B). IgE levels (C) and airway reactivity (D) following sensitization to ovalbumin in animals treated with the same amount of $PM_{2.5}$ from Hettsted or Zerbst.



Impact and Outcomes

The EPA Asthma Program as it focuses on PM has had a substantial impact. Impact to date from these studies and others include:

- Better understanding of the relationship between exposure to PM and its components, as well as local point sources and proximity to roadways, to airway inflammation in asthmatics.
- Appreciation of the role of innate immunity in response of asthmatics to PM.
- Asthmatics have enhanced deposition of PM which could partially explain their susceptibility.
- Appreciation for the role of inhaled corticosteroids in mitigating the impact of PM, and potential for other agents as well, such as antioxidants and anti-leukotrienes.

Future Directions

- Develop new biomarkers of risk and exposure in asthmatics using cutting edge molecular genetics approaches.
- Better understand differences in airway physiology between asthmatics and healthy people, as they relate to air pollution.
- Identify mechanisms which underlie the response of asthmatics to PM.
- Identify potential intervention strategies to better protect asthmatics from PM.

Impact and Outcomes

The results of these studies are used by the OAR for hazard identification and risk, and benefits assessment purposes. Most recently the data has also served to develop new educational materials, and programs which support health messages for the Air Quality Index.

Health and Exposure